Attorney Docket No.:28967/34891A

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| Applicants: Alitalo <i>et al.</i> | ) | EXPRESS MAIL LABEL NO.:              |
|-----------------------------------|---|--------------------------------------|
|                                   | ) | EM578445010US                        |
| Serial No.: Not yet assigned      | ) |                                      |
|                                   | ) | I hereby certify that this paper and |
| Filed: Herewith                   | ) | the documents referred to as         |
|                                   | ) | enclosed herewith are being          |
| For: Flt4 (VEGFR-3) as a Target   | ) | deposited with the United States     |
| for Tumor Imaging and Anti-Tumor  | ) | Postal Service as "EXPRESS MAIL      |
| Therapy                           | ) | POST OFFICE TO ADDRESSEE"            |
|                                   | ) | Service under 37 C.F.R. §1.10 on     |
| Group Art Unit: Not yet assigned  | } | the date indicated below and is      |
|                                   | ) | addressed to: Commissioner for       |
| Examiner: Not yet assigned        | ) | Patents, Box Patent Application,     |
| , <u>-</u>                        | ) | Washington, D.C. 20231 on this       |
|                                   | ) | date:                                |
|                                   | ) |                                      |
|                                   | ) | January 19, 2001                     |
|                                   | ) | S 1 -a M                             |
|                                   | ) | Mon                                  |
|                                   | ) | David A. Gass                        |
|                                   | , |                                      |

## STATEMENT PURSUANT TO 37 C.F.R. § 1.921(f)

Commissioner for Patents **Box Patent Application** Washington, D.C. 20231

Sir:

I hereby state that the content of the paper and computer readable forms of the sequence listing that is part of the above-identified application and that are filed herewith are the same.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN, **MURRAY & BORUN** 6300 Sears Tower 233 South Wacker Drive Chicago, Illinois 60606-6402 (312) 474-6300

January 19, 2001

By:

David A. Gass Reg. No: 38,153

## SEQUENCE LISTING

| <110>                     | Alital<br>Kaipai<br>Valtol<br>Jussil | nen,<br>a, Re    | Arja<br>eija | L               |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
|---------------------------|--------------------------------------|------------------|--------------|-----------------|------------------|------------------|------------------|-----------------|------------|------------------|------------------|------------|----------------------|------------|---------|
| <120>E                    | Flt4 (V                              | EGFR             | -3) a        | ıs a            | Targ             | et f             | or 5             | [umor           | Ima        | aging            | and              | An         | ti-Tu                | mor        | Therapy |
| <130>                     | 28113/                               | 3489             | 1            |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <140><br><141>            |                                      |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
|                           | 08/901<br>1997-0                     |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
|                           | 08/340<br>1994-1                     |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
|                           | 08/257<br>1994-0                     |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
|                           | 07/959<br>1992-1                     |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <160>                     | 22                                   |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <170>                     | Patent                               | :In V            | er.          | 2.0             |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <210><211><211><212><213> | 4195                                 | sapie            | ns           |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <220><221><222>           |                                      | .(391            | .3)          |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |
| <400><br>ccacg            | 1<br>cgcag                           | cggcc            | :ggag        | atg<br>Met<br>1 | Gln              | cgg<br>Arg       | ggc              | gcc<br>Ala<br>5 | Ala        | ctg<br>Leu       | tgc<br>Cys       | cto        | g cga<br>1 Arg<br>10 | ьeu        | 52      |
| tgg c<br>Trp L            | tc tgc<br>eu Cys                     | ctg<br>Leu<br>15 | gga<br>Gly   | ctc<br>Leu      | ctg<br>Leu       | Asp              | ggc<br>Gly<br>20 | Leu             | Val        | agt<br>Ser       | Gly              | Tyr        | Ser                  | atg<br>Met | 100     |
| acc c<br>Thr P            | cc ccg<br>ro Pro<br>30               | Thr              | ttg<br>Leu   | aac<br>Asn      | atc<br>Ile       | acg<br>Thr<br>35 | gag<br>Glu       | gag<br>Glu      | tca<br>Ser | cac<br>His       | gtc<br>Val<br>40 | atc<br>Ile | gac<br>Asp           | acc<br>Thr | 148     |
| ggt g<br>Gly A            | gac agc<br>Asp Ser<br>45             | ctg<br>Leu       | tcc<br>Ser   | atc<br>Ile      | tcc<br>Ser<br>50 | tgc<br>Cys       | agg<br>Arg       | gga<br>Gly      | cag<br>Gln | cac<br>His<br>55 | ccc<br>Pro       | ctc<br>Leu | gag<br>Glu           | tgg<br>Trp | 196     |
|                           |                                      |                  |              |                 |                  |                  |                  |                 |            |                  |                  |            |                      |            |         |

| gct<br>Ala<br>60  | tgg<br>Trp        | cca<br>Pro        | gga<br>Gly        | gct<br>Ala        | cag<br>Gln<br>65  | gag<br>Glu        | gcg<br>Ala        | cca<br>Pro        | gcc<br>Ala        | acc<br>Thr<br>70  | gga<br>Gly        | gac<br>Asp        | aag<br>Lys        | gac<br>Asp        | agc<br>Ser<br>75  | 244 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| gag<br>Glu        | gac<br>Asp        | acg<br>Thr        | gly<br>ggg        | gtg<br>Val<br>80  | gtg<br>Val        | cga<br>Arg        | gac<br>Asp        | tgc<br>Cys        | gag<br>Glu<br>85  | ggc<br>Gly        | aca<br>Thr        | gac<br>Asp        | gcc<br>Ala        | agg<br>Arg<br>90  | ccc<br>Pro        | 292 |
| tac<br>Tyr        | tgc<br>Cys        | aag<br>Lys        | gtg<br>Val<br>95  | ttg<br>Leu        | ctg<br>Leu        | ctg<br>Leu        | cac<br>His        | gag<br>Glu<br>100 | gta<br>Val        | cat<br>His        | gcc<br>Ala        | aac<br>Asn        | gac<br>Asp<br>105 | aca<br>Thr        | ggc<br>Gly        | 340 |
| agc<br>Ser        | tac<br>Tyr        | gtc<br>Val<br>110 | tgc<br>Cys        | tac<br>Tyr        | tac<br>Tyr        | aag<br>Lys        | tac<br>Tyr<br>115 | atc<br>Ile        | aag<br>Lys        | gca<br>Ala        | cgc<br>Arg        | atc<br>Ile<br>120 | gag<br>Glu        | ggc<br>Gly        | acc<br>Thr        | 388 |
| acg<br>Thr        | gcc<br>Ala<br>125 | gcc<br>Ala        | agc<br>Ser        | tcc<br>Ser        | tac<br>Tyr        | gtg<br>Val<br>130 | ttc<br>Phe        | gtg<br>Val        | aga<br>Arg        | gac<br>Asp        | ttt<br>Phe<br>135 | gag<br>Glu        | cag<br>Gln        | cca<br>Pro        | ttc<br>Phe        | 436 |
| atc<br>Ile<br>140 | aac<br>Asn        | aag<br>Lys        | cct<br>Pro        | gac<br>Asp        | acg<br>Thr<br>145 | ctc<br>Leu        | ttg<br>Leu        | gtc<br>Val        | aac<br>Asn        | agg<br>Arg<br>150 | aag<br>Lys        | gac<br>Asp        | gcc<br>Ala        | atg<br>Met        | tgg<br>Trp<br>155 | 484 |
| gtg<br>Val        | ccc<br>Pro        | tgt<br>Cys        | ctg<br>Leu        | gtg<br>Val<br>160 | tcc<br>Ser        | atc<br>Ile        | ccc<br>Pro        | ggc<br>Gly        | ctc<br>Leu<br>165 | aat<br>Asn        | gtc<br>Val        | acg<br>Thr        | ctg<br>Leu        | cgc<br>Arg<br>170 | tcg<br>Ser        | 532 |
| caa<br>Gln        | agc<br>Ser        | tcg<br>Ser        | gtg<br>Val<br>175 | ctg<br>Leu        | tgg<br>Trp        | cca<br>Pro        | gac<br>Asp        | 999<br>Gly<br>180 | cag<br>Gln        | gag<br>Glu        | gtg<br>Val        | gtg<br>Val        | tgg<br>Trp<br>185 | gat<br>Asp        | gac<br>Asp        | 580 |
| cgg<br>Arg        | cgg<br>Arg        | ggc<br>Gly<br>190 | atg<br>Met        | ctc<br>Leu        | gtg<br>Val        | tcc<br>Ser        | acg<br>Thr<br>195 | cca<br>Pro        | ctg<br>Leu        | ctg<br>Leu        | cac<br>His        | gat<br>Asp<br>200 | gcc<br>Ala        | ctg<br>Leu        | tac<br>Tyr        | 628 |
| ctg<br>Leu        | cag<br>Gln<br>205 | tgc<br>Cys        | gag<br>Glu        | acc<br>Thr        | acc<br>Thr        | tgg<br>Trp<br>210 | gga<br>Gly        | gac<br>Asp        | cag<br>Gln        | gac<br>Asp        | ttc<br>Phe<br>215 | ctt<br>Leu        | tcc<br>Ser        | aac<br>Asn        | ccc<br>Pro        | 676 |
| ttc<br>Phe<br>220 | ctg<br>Leu        | gtg<br>Val        | cac<br>His        | atc<br>Ile        | aca<br>Thr<br>225 | ggc<br>Gly        | aac<br>Asn        | gag<br>Glu        | ctc<br>Leu        | tat<br>Tyr<br>230 | gac<br>Asp        | atc<br>Ile        | cag<br>Gln        | ctg<br>Leu        | ttg<br>Leu<br>235 | 724 |
| ccc<br>Pro        | agg<br>Arg        | aag<br>Lys        | tcg<br>Ser        | ctg<br>Leu<br>240 | gag<br>Glu        | ctg<br>Leu        | ctg<br>Leu        | gta<br>Val        | 999<br>Gly<br>245 | gag<br>Glu        | aag<br>Lys        | ctg<br>Leu        | gtc<br>Val        | ctg<br>Leu<br>250 | aac<br>Asn        | 772 |

| tgc<br>Cys        | acc<br>Thr        | gtg<br>Val        | tgg<br>Trp<br>255 | gct<br>Ala        | gag<br>Glu        | ttt<br>Phe        | aac<br>Asn        | tca<br>Ser<br>260 | ggt<br>Gly        | gtc<br>Val        | acc<br>Thr        | ttt<br>Phe        | gac<br>Asp<br>265 | tgg<br>Trp        | gac<br>Asp        | 820  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tac<br>Tyr        | cca<br>Pro        | 999<br>Gly<br>270 | aag<br>Lys        | cag<br>Gln        | gca<br>Ala        | gag<br>Glu        | cgg<br>Arg<br>275 | ggt<br>Gly        | aag<br>Lys        | tgg<br>Trp        | gtg<br>Val        | ccc<br>Pro<br>280 | gag<br>Glu        | cga<br>Arg        | cgc<br>Arg        | 868  |
| tcc<br>Ser        | cag<br>Gln<br>285 | cag<br>Gln        | acc<br>Thr        | cac<br>His        | aca<br>Thr        | gaa<br>Glu<br>290 | ctc<br>Leu        | tcc<br>Ser        | agc<br>Ser        | atc<br>Ile        | ctg<br>Leu<br>295 | acc<br>Thr        | atc<br>Ile        | cac<br>His        | aac<br>Asn        | 916  |
| gtc<br>Val<br>300 | agc<br>Ser        | cag<br>Gln        | cac<br>His        | gac<br>Asp        | ctg<br>Leu<br>305 | ggc<br>Gly        | tcg<br>Ser        | tat<br>Tyr        | gtg<br>Val        | tgc<br>Cys<br>310 | aag<br>Lys        | gcc<br>Ala        | aac<br>Asn        | aac<br>Asn        | ggc<br>Gly<br>315 | 964  |
| atc<br>Ile        | cag<br>Gln        | cga<br>Arg        | ttt<br>Phe        | cgg<br>Arg<br>320 | gag<br>Glu        | agc<br>Ser        | acc<br>Thr        | gag<br>Glu        | gtc<br>Val<br>325 | att<br>Ile        | gtg<br>Val        | cat<br>His        | gaa<br>Glu        | aat<br>Asn<br>330 | ccc<br>Pro        | 1012 |
| ttc<br>Phe        | atc<br>Ile        | agc<br>Ser        | gtc<br>Val<br>335 | gag<br>Glu        | tgg<br>Trp        | ctc<br>Leu        | aaa<br>Lys        | gga<br>Gly<br>340 | ccc<br>Pro        | atc<br>Ile        | ctg<br>Leu        | gag<br>Glu        | gcc<br>Ala<br>345 | acg<br>Thr        | gca<br>Ala        | 1060 |
| gga<br>Gly        | gac<br>Asp        | gag<br>Glu<br>350 | ctg<br>Leu        | gtg<br>Val        | aag<br>Lys        | ctg<br>Leu        | ccc<br>Pro<br>355 | gtg<br>Val        | aag<br>Lys        | ctg<br>Leu        | gca<br>Ala        | gcg<br>Ala<br>360 | tac<br>Tyr        | ccc<br>Pro        | ccg<br>Pro        | 1108 |
| ccc<br>Pro        | gag<br>Glu<br>365 | ttc<br>Phe        | cag<br>Gln        | tgg<br>Trp        | tac<br>Tyr        | aag<br>Lys<br>370 | gat<br>Asp        | gga<br>Gly        | aag<br>Lys        | gca<br>Ala        | ctg<br>Leu<br>375 | tcc<br>Ser        | gly<br>aaa        | cgc<br>Arg        | cac<br>His        | 1156 |
| agt<br>Ser<br>380 | cca<br>Pro        | cat<br>His        | gcc<br>Ala        | ctg<br>Leu        | gtg<br>Val<br>385 | ctc<br>Leu        | aag<br>Lys        | gag<br>Glu        | gtg<br>Val        | aca<br>Thr<br>390 | gag<br>Glu        | gcc<br>Ala        | agc<br>Ser        | aca<br>Thr        | ggc<br>Gly<br>395 | 1204 |
| acc<br>Thr        | tac<br>Tyr        | acc<br>Thr        | ctc<br>Leu        | gcc<br>Ala<br>400 | ctg<br>Leu        | tgg<br>Trp        | aac<br>Asn        | tcc<br>Ser        | gct<br>Ala<br>405 | gct<br>Ala        | ggc<br>Gly        | ctg<br>Leu        | agg<br>Arg        | cgc<br>Arg<br>410 | aac<br>Asn        | 1252 |
| atc<br>Ile        | agc<br>Ser        | ctg<br>Leu        | gag<br>Glu<br>415 | ctg<br>Leu        | gtg<br>Val        | gtg<br>Val        | aat<br>Asn        | gtg<br>Val<br>420 | ccc<br>Pro        | ccc<br>Pro        | cag<br>Gln        | ata<br>Ile        | cat<br>His<br>425 | gag<br>Glu        | aag<br>Lys        | 1300 |
| gag<br>Glu        | gcc<br>Ala        | tcc<br>Ser<br>430 | tcc<br>Ser        | ccc<br>Pro        | agc<br>Ser        | atc<br>Ile        | tac<br>Tyr<br>435 | tcg<br>Ser        | cgt<br>Arg        | cac<br>His        | agc<br>Ser        | cgc<br>Arg<br>440 | cag<br>Gln        | gcc<br>Ala        | ctc<br>Leu        | 1348 |
| acc<br>Thr        | tgc<br>Cys<br>445 | acg<br>Thr        | gcc<br>Ala        | tac<br>Tyr        | gly<br>aaa        | gtg<br>Val<br>450 | ccc<br>Pro        | ctg<br>Leu        | cct<br>Pro        | ctc<br>Leu        | agc<br>Ser<br>455 | Ile               | cag<br>Gln        | tgg<br>Trp        | cac<br>His        | 1396 |

| tgg<br>Trp<br>460 | cgg<br>Arg | ccc<br>Pro | tgg<br>Trp | aca<br>Thr | ccc<br>Pro<br>465 | tgc<br>Cys        | aag<br>Lys | atg<br>Met | ttt<br>Phe | gcc<br>Ala<br>470 | cag<br>Gln | cgt<br>Arg | agt<br>Ser | ctc<br>Leu | cgg<br>Arg<br>475 | 1444 |
|-------------------|------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------|
|                   |            |            |            |            |                   | ctc<br>Leu        |            |            |            |                   |            |            |            |            |                   | 1492 |
|                   |            |            |            |            |                   | gtg<br>Val        |            |            |            |                   |            |            |            |            |                   | 1540 |
|                   |            |            |            |            |                   | aag<br>Lys        |            |            |            |                   |            |            |            |            |                   | 1588 |
| _                 |            | _          |            |            |                   | gcc<br>Ala<br>530 | _          |            | _          | _                 |            |            |            |            | _                 | 1636 |
|                   |            |            |            |            |                   | ctc<br>Leu        |            |            |            |                   |            |            |            |            |                   | 1684 |
|                   |            |            |            |            |                   | tcc<br>Ser        |            |            |            |                   |            |            |            |            |                   | 1732 |
| _                 | _          |            |            |            | _                 | tgc<br>Cys        |            | _          | _          | _                 |            | _          |            | _          |                   | 1780 |
| _                 | _          |            |            | _          |                   | aac<br>Asn        | _          |            | _          | _                 |            | _          |            |            |                   | 1828 |
|                   |            |            |            |            |                   | tgc<br>Cys<br>610 |            |            |            |                   |            |            |            |            |                   | 1876 |
| _                 | _          | _          | _          | _          |                   | gag<br>Glu        |            | _          |            |                   |            |            |            |            |                   | 1924 |
|                   |            |            |            |            |                   | cgc<br>Arg        |            |            |            |                   |            |            |            |            |                   | 1972 |
|                   |            |            |            |            |                   | cgg<br>Arg        |            |            |            |                   |            |            |            |            |                   | 2020 |

| aag<br>Lys        | tac<br>Tyr        | ctg<br>Leu<br>670 | tcg<br>Ser        | gtg<br>Val        | cag<br>Gln        | gcc<br>Ala        | ctg<br>Leu<br>675 | gaa<br>Glu        | gcc<br>Ala        | cct<br>Pro        | cgg<br>Arg        | ctc<br>Leu<br>680 | acg<br>Thr        | cag<br>Gln        | aac<br>Asn        | 2068 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| ttg<br>Leu        | acc<br>Thr<br>685 | gac<br>Asp        | ctc<br>Leu        | ctg<br>Leu        | gtg<br>Val        | aac<br>Asn<br>690 | gtg<br>Val        | agc<br>Ser        | gac<br>Asp        | tcg<br>Ser        | ctg<br>Leu<br>695 | gag<br>Glu        | atg<br>Met        | cag<br>Gln        | tgc<br>Cys        | 2116 |
| ttg<br>Leu<br>700 | gtg<br>Val        | gcc<br>Ala        | gga<br>Gly        | gcg<br>Ala        | cac<br>His<br>705 | gcg<br>Ala        | ccc<br>Pro        | agc<br>Ser        | atc<br>Ile        | gtg<br>Val<br>710 | tgg<br>Trp        | tac<br>Tyr        | aaa<br>Lys        | gac<br>Asp        | gag<br>Glu<br>715 | 2164 |
| agg<br>Arg        | ctg<br>Leu        | ctg<br>Leu        | gag<br>Glu        | gaa<br>Glu<br>720 | aag<br>Lys        | tct<br>Ser        | gga<br>Gly        | gtc<br>Val        | gac<br>Asp<br>725 | ttg<br>Leu        | gcg<br>Ala        | gac<br>Asp        | tcc<br>Ser        | aac<br>Asn<br>730 | cag<br>Gln        | 2212 |
| aag<br>Lys        | ctg<br>Leu        | agc<br>Ser        | atc<br>Ile<br>735 | cag<br>Gln        | cgc<br>Arg        | gtg<br>Val        | cgc<br>Arg        | gag<br>Glu<br>740 | gag<br>Glu        | gat<br>Asp        | gcg<br>Ala        | gga<br>Gly        | cgc<br>Arg<br>745 | tat<br>Tyr        | ctg<br>Leu        | 2260 |
| tgc<br>Cys        | agc<br>Ser        | gtg<br>Val<br>750 | tgc<br>Cys        | aac<br>Asn        | gcc<br>Ala        | aag<br>Lys        | ggc<br>Gly<br>755 | tgc<br>Cys        | gtc<br>Val        | aac<br>Asn        | tcc<br>Ser        | tcc<br>Ser<br>760 | gcc<br>Ala        | agc<br>Ser        | gtg<br>Val        | 2308 |
| gcc<br>Ala        | gtg<br>Val<br>765 | gaa<br>Glu        | ggc<br>Gly        | tcc<br>Ser        | gag<br>Glu        | gat<br>Asp<br>770 | aag<br>Lys        | ggc<br>Gly        | agc<br>Ser        | atg<br>Met        | gag<br>Glu<br>775 | atc<br>Ile        | gtg<br>Val        | atc<br>Ile        | ctt<br>Leu        | 2356 |
| gtc<br>Val<br>780 | ggt<br>Gly        | acc<br>Thr        | ggc<br>Gly        | gtc<br>Val        | atc<br>Ile<br>785 | gct<br>Ala        | gtc<br>Val        | ttc<br>Phe        | ttc<br>Phe        | tgg<br>Trp<br>790 | gtc<br>Val        | ctc<br>Leu        | ctc<br>Leu        | ctc<br>Leu        | ctc<br>Leu<br>795 | 2404 |
| atc<br>Ile        | ttc<br>Phe        | tgt<br>Cys        | aac<br>Asn        | atg<br>Met<br>800 | agg<br>Arg        | agg<br>Arg        | ccg<br>Pro        | gcc<br>Ala        | cac<br>His<br>805 | gca<br>Ala        | gac<br>Asp        | atc<br>Ile        | aag<br>Lys        | acg<br>Thr<br>810 | ggc<br>Gly        | 2452 |
| tac<br>Tyr        | ctg<br>Leu        | tcc<br>Ser        | atc<br>Ile<br>815 | atc<br>Ile        | atg<br>Met        | gac<br>Asp        | ccc<br>Pro        | 999<br>Gly<br>820 | gag<br>Glu        | gtg<br>Val        | cct<br>Pro        | ctg<br>Leu        | gag<br>Glu<br>825 | gag<br>Glu        | caa<br>Gln        | 2500 |
| tgc<br>Cys        | gaa<br>Glu        | tac<br>Tyr<br>830 | ctg<br>Leu        | tcc<br>Ser        | tac<br>Tyr        | gat<br>Asp        | gcc<br>Ala<br>835 | agc<br>Ser        | cag<br>Gln        | tgg<br>Trp        | gaa<br>Glu        | ttc<br>Phe<br>840 | ccc<br>Pro        | cga<br>Arg        | gag<br>Glu        | 2548 |
| cgg<br>Arg        | ctg<br>Leu<br>845 | cac<br>His        | ctg<br>Leu        | Gly<br>aaa        | aga<br>Arg        | gtg<br>Val<br>850 | ctc<br>Leu        | ggc               | tac<br>Tyr        | Gly               | gcc<br>Ala<br>855 | ttc<br>Phe        | gly<br>aaa        | aag<br>Lys        | gtg<br>Val        | 2596 |
| gtg<br>Val<br>860 | gaa<br>Glu        | gcc<br>Ala        | tcc<br>Ser        | gct<br>Ala        | ttc<br>Phe<br>865 | ggc<br>Gly        | atc<br>Ile        | cac<br>His        | aag<br>Lys        | ggc<br>Gly<br>870 | Ser               | agc<br>Ser        | tgt<br>Cys        | gac<br>Asp        | acc<br>Thr<br>875 | 2644 |

|                                    |                                    |                            | gcc acg gcc<br>Ala Thr Ala<br>885  |                            | a Arg                       |
|------------------------------------|------------------------------------|----------------------------|------------------------------------|----------------------------|-----------------------------|
|                                    | 0 0 0                              | _                          | att cac atc<br>Ile His Ile         |                            |                             |
|                                    |                                    |                            | acc aag ccg<br>Thr Lys Pro         |                            |                             |
|                                    |                                    |                            | ggc aac ctc<br>Gly Asn Leu<br>935  |                            |                             |
|                                    |                                    |                            | tgc gcg gag<br>Cys Ala Glu<br>950  | _                          |                             |
|                                    |                                    |                            | gag ctc gcc<br>Glu Leu Ala<br>965  |                            | Arg                         |
|                                    |                                    |                            | ctc ttc gcg<br>Leu Phe Ala         |                            |                             |
|                                    |                                    |                            | cca gac caa<br>Pro Asp Gln         |                            |                             |
|                                    | Ser Pro Leu                        |                            | gat ctt gtc<br>Asp Leu Val<br>1015 |                            |                             |
| cag gtg gcc<br>Gln Val Ala<br>1020 | aga ggg atg<br>Arg Gly Met<br>1025 | gag ttc ctg<br>Glu Phe Leu | gct tcc cga<br>Ala Ser Arg<br>1030 | aag tgc ato<br>Lys Cys Ile | c cac 3124<br>e His<br>1035 |
|                                    |                                    | Asn Ile Leu                | ctg tcg gaa<br>Leu Ser Glu<br>1045 |                            | . Val                       |
| Lys Ile Cys                        |                                    |                            | gac atc tac<br>Asp Ile Tyr         |                            | _                           |
|                                    |                                    |                            | ccc ctg aag<br>Pro Leu Lys         |                            |                             |

| gaa agc atc<br>Glu Ser Ile<br>1085 | ttc gac aag<br>Phe Asp Lys         | gtg tac acc<br>Val Tyr Thr<br>1090 | acg cag agt<br>Thr Gln Ser<br>1095 | gac gtg tgg<br>Asp Val Trp            | tcc 3316<br>Ser |
|------------------------------------|------------------------------------|------------------------------------|------------------------------------|---------------------------------------|-----------------|
|                                    | ctt ctc tgg<br>Leu Leu Trp<br>1105 |                                    |                                    | Ala Ser Pro                           |                 |
| 3000                               | cag atc aat<br>Gln Ile Asn<br>1120 | Glu Glu Phe                        |                                    |                                       |                 |
| Thr Arg Met                        | agg gcc ccg<br>Arg Ala Pro<br>1135 |                                    | -                                  |                                       |                 |
| •                                  | tgc tgg tcc<br>Cys Trp Ser         |                                    | Lys Ala Arg                        | _                                     | _               |
|                                    | gag atc ctg<br>Glu Ile Leu         |                                    |                                    |                                       |                 |
|                                    | gag gtc tgc<br>Glu Val Cys<br>1185 |                                    |                                    | Gln Ser Ser                           | -               |
|                                    | ttc tcg cag<br>Phe Ser Gln<br>1200 | Val Ser Thr                        |                                    | -                                     | _               |
|                                    | gag gac agc<br>Glu Asp Ser<br>1215 |                                    |                                    |                                       | _               |
|                                    | tac aac tgg<br>Tyr Asn Trp         |                                    | Pro Gly Cys                        |                                       |                 |
|                                    | cgt ggt tcc<br>Arg Gly Ser         |                                    |                                    |                                       |                 |
| _                                  | acg acc tac<br>Thr Thr Tyr<br>1265 |                                    |                                    | Gln Thr Asp                           | _               |
|                                    | ctg gcc tcg<br>Leu Ala Ser<br>1280 | Glu Glu Phe                        | ~ ~ ~                              | ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ |                 |

| aga caa gaa agc ggc ttc agg tagctgaagc agagagagag aaggcagcat<br>Arg Gln Glu Ser Gly Phe Arg<br>1295 | 3943 |
|---|------|
| acgtcagcat tttcttctct gcacttataa gaaagatcaa agactttaag actttcgcta                                   | 4003 |
| tttcttctac tgctatctac tacaaacttc aaagaggaac caggaggaca agaggagcat                                   | 4063 |
| gaaagtggac aaggagtgtg accactgaag caccacaggg aaggggttag gcctccggat                                   | 4123 |
| gactgcgggc aggcctggat aatatccagc ctcccacaag aagctggtgg agcagagtgt                                   | 4183 |
| tecetgaete et   | 4195 |
| <210> 2 <211> 1298 <212> PRT <213> Homo sapiens   |      |
| <pre>&lt;400&gt; 2 Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly 1 5 10 15</pre>  |      |
| Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu<br>20 25 30                         |      |
| Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser<br>35 40 45                         |      |
| Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala<br>50 55 60                         |      |
| Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val<br>65 70 75 80                      |      |
| Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu<br>85 90 95                         |      |
| Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr<br>100 105 110                      |      |
| Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser<br>115 120 125                      |      |
| Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp<br>130 135 140                      |      |
| Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val<br>145 150 155 160                  |      |
| Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu<br>165 170 175                      |      |
| Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu                                     |      |

Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr 195 200 205

- Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile 210 215 220
- Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu 225 230 235 240
- Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala 245 250 255
- Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
  260 265 270
- Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His 275 280 285
- Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp 290 295 300
- Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg 305 310 315 320
- Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu 325 330 335
- Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val\$340\$ \$345\$ 350
- Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp 355 360 365
- Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu 370 375 380
- Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala 385 390 395 400
- Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu 405 410 415
- Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
  425 430
- Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
  435 440 445

Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr 455 Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln 470 Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp 490 485 Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val 520 Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu 535 Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg 585 Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu 600 Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile 635 630 Pro Arq Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val 660 665 Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu 680 Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu 710 715 Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln Arg Val Arg Glu Glu Asp Ala Gly Arg Tyr Leu Cys Ser Val Cys Asn Ala Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser

760

765

755

- Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val 770 780
- Ile Ala Val Phe Phe Trp Val Leu Leu Leu Ile Phe Cys Asn Met 785 790 795 800
- Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile 805 810 815
- Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser 820 825 830
- Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
  835 840 845
- Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala 850 860
- Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met 865 870 875 880
- Leu Lys Glu Gly Ala Thr Ala Ser Glu His Arg Ala Leu Met Ser Glu 885 890 895
- Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu 900 905 910
- Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu 915 920 925
- Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp 930 940
- Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe 945 950 955 960
- Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser 965 970 975
- Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala 980 985 990
- Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro 995 1000 1005
- Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg Gly 1010 1015 1020
- Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala 025 1030 1035 1040
- Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile Cys Asp Phe 1045 1050 1055
- Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
  1060 1070
- Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asp \$1075\$ \$1080\$ \$1085

Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu 1090 1095 1100

Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile 105 1110 1115 1120

Asn Glu Glu Phe Cys Gln Arg Leu Arg Asp Gly Thr Arg Met Arg Ala 1125 1130 1135

Pro Glu Leu Ala Thr Pro Ala Ile Arg Arg Ile Met Leu Asn Cys Trp 1140 1145 1150

Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Glu Leu Val Glu Ile 1155 1160 1165

Leu Gly Asp Leu Gln Gly Arg Gly Leu Gln Glu Glu Glu Val 1170 1175 1180

Cys Met Ala Pro Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser 185 1190 1195 1200

Gln Val Ser Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp 1205 1210 1215

Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn 1220 1225 1230

Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly 1235 1240 1245

Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr Thr 1250 1260

Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala 265 1270 1275 1280

Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln Glu Ser Gly 1285 1290 1295

Phe Arg

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Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu

10

tgg ctc tgc ctg gga ctc ctg gac ggc ctg gtg agt ggc tac tcc atg Trp Leu Cys Leu Gly Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met 15 20 25

100

| acc<br>Thr       | ccc<br>Pro        | ccg<br>Pro<br>30  | acc<br>Thr        | ttg<br>Leu        | aac<br>Asn       | atc<br>Ile        | acg<br>Thr<br>35  | gag<br>Glu        | gag<br>Glu       | tca<br>Ser       | cac<br>His        | gtc<br>Val<br>40  | atc<br>Ile        | gac<br>Asp       | acc<br>Thr       | 148 |
|------------------|-------------------|-------------------|-------------------|-------------------|------------------|-------------------|-------------------|-------------------|------------------|------------------|-------------------|-------------------|-------------------|------------------|------------------|-----|
| ggt<br>Gly       | gac<br>Asp<br>45  | agc<br>Ser        | ctg<br>Leu        | tcc<br>Ser        | atc<br>Ile       | tcc<br>Ser<br>50  | tgc<br>Cys        | agg<br>Arg        | gga<br>Gly       | cag<br>Gln       | cac<br>His<br>55  | ccc<br>Pro        | ctc<br>Leu        | gag<br>Glu       | tgg<br>Trp       | 196 |
| gct<br>Ala<br>60 | tgg<br>Trp        | cca<br>Pro        | gga<br>Gly        | gct<br>Ala        | cag<br>Gln<br>65 | gag<br>Glu        | gcg<br>Ala        | cca<br>Pro        | gcc<br>Ala       | acc<br>Thr<br>70 | gga<br>Gly        | gac<br>Asp        | aag<br>Lys        | gac<br>Asp       | agc<br>Ser<br>75 | 244 |
| gag<br>Glu       | gac<br>Asp        | acg<br>Thr        | gly<br>aaa        | gtg<br>Val<br>80  | gtg<br>Val       | cga<br>Arg        | gac<br>Asp        | tgc<br>Cys        | gag<br>Glu<br>85 | ggc              | aca<br>Thr        | gac<br>Asp        | gcc<br>Ala        | agg<br>Arg<br>90 | ccc<br>Pro       | 292 |
| tac<br>Tyr       | tgc<br>Cys        | aag<br>Lys        | gtg<br>Val<br>95  | ttg<br>Leu        | ctg<br>Leu       | ctg<br>Leu        | cac<br>His        | gag<br>Glu<br>100 | gta<br>Val       | cat<br>His       | gcc<br>Ala        | aac<br>Asn        | gac<br>Asp<br>105 | aca<br>Thr       | ggc              | 340 |
| agc<br>Ser       | tac<br>Tyr        | gtc<br>Val<br>110 | tgc<br>Cys        | tac<br>Tyr        | tac<br>Tyr       | aag<br>Lys        | tac<br>Tyr<br>115 | atc<br>Ile        | aag<br>Lys       | gca<br>Ala       | cgc<br>Arg        | atc<br>Ile<br>120 | gag<br>Glu        | ggc<br>Gly       | acc<br>Thr       | 388 |
| acg<br>Thr       | gcc<br>Ala<br>125 | gcc<br>Ala        | agc<br>Ser        | tcc<br>Ser        | tac<br>Tyr       | gtg<br>Val<br>130 | ttc<br>Phe        | gtg<br>Val        | aga<br>Arg       | gac<br>Asp       | ttt<br>Phe<br>135 | gag<br>Glu        | cag<br>Gln        | cca<br>Pro       | ttc<br>Phe       | 436 |
|                  |                   |                   |                   | gac<br>Asp        |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 484 |
|                  |                   |                   |                   | gtg<br>Val<br>160 |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 532 |
|                  |                   |                   |                   | ctg<br>Leu        |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 580 |
|                  |                   |                   |                   | ctc<br>Leu        |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 628 |
| ctg<br>Leu       | cag<br>Gln<br>205 | tgc<br>Cys        | gag<br>Glu        | acc<br>Thr        | acc<br>Thr       | tgg<br>Trp<br>210 | gga<br>Gly        | gac<br>Asp        | cag<br>Gln       | gac<br>Asp       | ttc<br>Phe<br>215 | ctt<br>Leu        | tcc<br>Ser        | aac<br>Asn       | ccc<br>Pro       | 676 |
|                  |                   |                   |                   | atc<br>Ile        |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 724 |
|                  |                   |                   |                   | ctg<br>Leu<br>240 |                  |                   |                   |                   |                  |                  |                   |                   |                   |                  |                  | 772 |
| tgc<br>Cys       | acc<br>Thr        | gtg<br>Val        | tgg<br>Trp<br>255 | gct<br>Ala        | gag<br>Glu       | ttt<br>Phe        | aac<br>Asn        | tca<br>Ser<br>260 | ggt<br>Gly       | gtc<br>Val       | acc<br>Thr        | ttt<br>Phe        | gac<br>Asp<br>265 | tgg<br>Trp       | gac<br>Asp       | 820 |

| tac<br>Tyr        | cca<br>Pro        | 999<br>Gly<br>270 | aag<br>Lys        | cag<br>Gln        | gca<br>Ala        | gag<br>Glu        | cgg<br>Arg<br>275 | ggt<br>Gly        | aag<br>Lys        | tgg<br>Trp        | gtg<br>Val        | ccc<br>Pro<br>280 | gag<br>Glu        | cga<br>Arg        | cgc<br>Arg        | 868  |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| tcc<br>Ser        | cag<br>Gln<br>285 | cag<br>Gln        | acc<br>Thr        | cac<br>His        | aca<br>Thr        | gaa<br>Glu<br>290 | ctc<br>Leu        | tcc<br>Ser        | agc<br>Ser        | atc<br>Ile        | ctg<br>Leu<br>295 | acc<br>Thr        | atc<br>Ile        | cac<br>His        | aac<br>Asn        | 916  |
| gtc<br>Val<br>300 | agc<br>Ser        | cag<br>Gln        | cac<br>His        | gac<br>Asp        | ctg<br>Leu<br>305 | ggc<br>Gly        | tcg<br>Ser        | tat<br>Tyr        | gtg<br>Val        | tgc<br>Cys<br>310 | aag<br>Lys        | gcc<br>Ala        | aac<br>Asn        | aac<br>Asn        | ggc<br>Gly<br>315 | 964  |
| atc<br>Ile        | cag<br>Gln        | cga<br>Arg        | ttt<br>Phe        | cgg<br>Arg<br>320 | gag<br>Glu        | agc<br>Ser        | acc<br>Thr        | gag<br>Glu        | gtc<br>Val<br>325 | att<br>Ile        | gtg<br>Val        | cat<br>His        | gaa<br>Glu        | aat<br>Asn<br>330 | ccc<br>Pro        | 1012 |
| ttc<br>Phe        | atc<br>Ile        | agc<br>Ser        | gtc<br>Val<br>335 | gag<br>Glu        | tgg<br>Trp        | ctc<br>Leu        | aaa<br>Lys        | gga<br>Gly<br>340 | ccc<br>Pro        | atc<br>Ile        | ctg<br>Leu        | gag<br>Glu        | gcc<br>Ala<br>345 | acg<br>Thr        | gca<br>Ala        | 1060 |
| gga<br>Gly        | gac<br>Asp        | gag<br>Glu<br>350 | ctg<br>Leu        | gtg<br>Val        | aag<br>Lys        | ctg<br>Leu        | ccc<br>Pro<br>355 | gtg<br>Val        | aag<br>Lys        | ctg<br>Leu        | gca<br>Ala        | gcg<br>Ala<br>360 | tac<br>Tyr        | ccc<br>Pro        | ccg<br>Pro        | 1108 |
| ccc<br>Pro        | gag<br>Glu<br>365 | ttc<br>Phe        | cag<br>Gln        | tgg<br>Trp        | tac<br>Tyr        | aag<br>Lys<br>370 | gat<br>Asp        | gga<br>Gly        | aag<br>Lys        | gca<br>Ala        | ctg<br>Leu<br>375 | tcc<br>Ser        | ggg<br>Gly        | cgc<br>Arg        | cac<br>His        | 1156 |
| agt<br>Ser<br>380 | cca<br>Pro        | cat<br>His        | gcc<br>Ala        | ctg<br>Leu        | gtg<br>Val<br>385 | ctc<br>Leu        | aag<br>Lys        | gag<br>Glu        | gtg<br>Val        | aca<br>Thr<br>390 | gag<br>Glu        | gcc<br>Ala        | agc<br>Ser        | aca<br>Thr        | ggc<br>Gly<br>395 | 1204 |
| acc<br>Thr        | tac<br>Tyr        | acc<br>Thr        | ctc<br>Leu        | gcc<br>Ala<br>400 | ctg<br>Leu        | tgg<br>Trp        | aac<br>Asn        | tcc<br>Ser        | gct<br>Ala<br>405 | gct<br>Ala        | ggc<br>Gly        | ctg<br>Leu        | agg<br>Arg        | cgc<br>Arg<br>410 | aac<br>Asn        | 1252 |
| atc<br>Ile        | agc<br>Ser        | ctg<br>Leu        | gag<br>Glu<br>415 | ctg<br>Leu        | gtg<br>Val        | gtg<br>Val        | aat<br>Asn        | gtg<br>Val<br>420 | ccc<br>Pro        | ccc<br>Pro        | cag<br>Gln        | ata<br>Ile        | cat<br>His<br>425 | gag<br>Glu        | aag<br>Lys        | 1300 |
| gag<br>Glu        | gcc<br>Ala        | tcc<br>Ser<br>430 | tcc<br>Ser        | ccc<br>Pro        | agc<br>Ser        | atc<br>Ile        | tac<br>Tyr<br>435 | tcg<br>Ser        | cgt<br>Arg        | cac<br>His        | agc<br>Ser        | cgc<br>Arg<br>440 | cag<br>Gln        | gcc<br>Ala        | ctc<br>Leu        | 1348 |
| acc<br>Thr        | tgc<br>Cys<br>445 | acg<br>Thr        | gcc<br>Ala        | tac<br>Tyr        | gly               | gtg<br>Val<br>450 | ccc<br>Pro        | ctg<br>Leu        | cct<br>Pro        | ctc<br>Leu        | agc<br>Ser<br>455 | Ile               | cag<br>Gln        | tgg<br>Trp        | cac<br>His        | 1396 |
| tgg<br>Trp<br>460 | cgg<br>Arg        | ccc<br>Pro        | tgg<br>Trp        | aca<br>Thr        | ccc<br>Pro<br>465 | tgc<br>Cys        | aag<br>Lys        | atg<br>Met        | ttt<br>Phe        | gcc<br>Ala<br>470 | Gln               | cgt<br>Arg        | agt<br>Ser        | ctc<br>Leu        | cgg<br>Arg<br>475 | 1444 |
| cgg<br>Arg        | cgg<br>Arg        | cag<br>Gln        | cag<br>Gln        | caa<br>Gln<br>480 | gac<br>Asp        | ctc<br>Leu        | atg<br>Met        | cca<br>Pro        | cag<br>Gln<br>485 | . Cys             | cgt<br>Arg        | gac<br>Asp        | tgg<br>Trp        | agg<br>Arg<br>490 | gcg<br>Ala        | 1492 |
| gtg<br>Val        | acc<br>Thr        | acg<br>Thr        | cag<br>Gln<br>495 | Asp               | gcc<br>Ala        | gtg<br>Val        | aac<br>Asn        | ccc<br>Pro<br>500 | Ile               | gag<br>Glu        | ago<br>Ser        | ctg<br>Leu        | gac<br>Asp<br>505 | Thr               | tgg<br>Trp        | 1540 |

| acc<br>Thr        | gag<br>Glu        | ttt<br>Phe<br>510 | gtg<br>Val        | gag<br>Glu | gga<br>Gly        | aag<br>Lys        | aat<br>Asn<br>515 | aag<br>Lys        | act<br>Thr | gtg<br>Val        | agc<br>Ser        | aag<br>Lys<br>520 | ctg<br>Leu        | gtg<br>Val | atc<br>Ile        | 1588 |
|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|------|
| cag<br>Gln        | aat<br>Asn<br>525 | gcc<br>Ala        | aac<br>Asn        | gtg<br>Val | tct<br>Ser        | gcc<br>Ala<br>530 | atg<br>Met        | tac<br>Tyr        | aag<br>Lys | tgt<br>Cys        | gtg<br>Val<br>535 | gtc<br>Val        | tcc<br>Ser        | aac<br>Asn | aag<br>Lys        | 1636 |
| gtg<br>Val<br>540 | ggc               | cag<br>Gln        | gat<br>Asp        | gag<br>Glu | cgg<br>Arg<br>545 | ctc<br>Leu        | atc<br>Ile        | tac<br>Tyr        | ttc<br>Phe | tat<br>Tyr<br>550 | gtg<br>Val        | acc<br>Thr        | acc<br>Thr        | atc<br>Ile | ccc<br>Pro<br>555 | 1684 |
|                   |                   |                   |                   |            |                   |                   |                   | cca<br>Pro        |            |                   |                   |                   |                   |            |                   | 1732 |
|                   |                   |                   |                   |            |                   |                   |                   | gcc<br>Ala<br>580 |            |                   |                   |                   |                   |            |                   | 1780 |
|                   |                   |                   |                   |            |                   |                   |                   | tcc<br>Ser        |            |                   |                   |                   |                   |            |                   | 1828 |
| aac<br>Asn        | ccg<br>Pro<br>605 | ctt<br>Leu        | ctg<br>Leu        | ctc<br>Leu | gac<br>Asp        | tgc<br>Cys<br>610 | aag<br>Lys        | aac<br>Asn        | gtg<br>Val | cat<br>His        | ctg<br>Leu<br>615 | ttc<br>Phe        | gcc<br>Ala        | acc<br>Thr | cct<br>Pro        | 1876 |
|                   |                   |                   |                   |            |                   |                   |                   | gca<br>Ala        |            |                   |                   |                   |                   |            |                   | 1924 |
|                   |                   |                   |                   |            |                   |                   |                   | gcg<br>Ala        |            |                   |                   |                   |                   |            |                   | 1972 |
|                   |                   |                   |                   |            |                   |                   |                   | agc<br>Ser<br>660 |            |                   |                   |                   |                   |            |                   | 2020 |
|                   |                   |                   |                   |            |                   |                   |                   | gaa<br>Glu        |            |                   |                   |                   |                   |            |                   | 2068 |
| ttg<br>Leu        | acc<br>Thr<br>685 | gac<br>Asp        | ctc<br>Leu        | ctg<br>Leu | gtg<br>Val        | aac<br>Asn<br>690 | gtg<br>Val        | agc<br>Ser        | gac<br>Asp | tcg<br>Ser        | ctg<br>Leu<br>695 | gag<br>Glu        | atg<br>Met        | cag<br>Gln | tgc<br>Cys        | 2116 |
|                   |                   |                   |                   |            |                   |                   |                   | agc<br>Ser        |            |                   |                   |                   |                   |            |                   | 2164 |
|                   |                   |                   |                   |            |                   |                   |                   | gtc<br>Val        |            |                   |                   |                   |                   |            |                   | 2212 |
| aag<br>Lys        | ctg<br>Leu        | agc<br>Ser        | atc<br>Ile<br>735 | cag<br>Gln | cgc<br>Arg        | gtg<br>Val        | cgc<br>Arg        | gag<br>Glu<br>740 | gag<br>Glu | gat<br>Asp        | gcg<br>Ala        | gga<br>Gly        | cgc<br>Arg<br>745 | tat<br>Tyr | ctg<br>Leu        | 2260 |

|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | agc<br>Ser        |                   | 2308 |
|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|------|
| gcc<br>Ala        | gtg<br>Val<br>765 | gaa<br>Glu        | ggc<br>Gly | tcc<br>Ser | gag<br>Glu        | gat<br>Asp<br>770 | aag<br>Lys        | ggc<br>Gly | agc<br>Ser | atg<br>Met        | gag<br>Glu<br>775 | atc<br>Ile        | gtg<br>Val | atc<br>Ile        | ctt<br>Leu        | 2356 |
| gtc<br>Val<br>780 | ggt<br>Gly        | acc<br>Thr        | ggc<br>Gly | gtc<br>Val | atc<br>Ile<br>785 | gct<br>Ala        | gtc<br>Val        | ttc<br>Phe | ttc<br>Phe | tgg<br>Trp<br>790 | gtc<br>Val        | ctc<br>Leu        | ctc<br>Leu | ctc<br>Leu        | ctc<br>Leu<br>795 | 2404 |
|                   |                   |                   |            | _          |                   |                   | -                 | _          |            | _                 | -                 |                   |            | acg<br>Thr<br>810 |                   | 2452 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | gag<br>Glu        |                   | 2500 |
| tgc<br>Cys        | gaa<br>Glu        | tac<br>Tyr<br>830 | ctg<br>Leu | tcc<br>Ser | tac<br>Tyr        | gat<br>Asp        | gcc<br>Ala<br>835 | agc<br>Ser | cag<br>Gln | tgg<br>Trp        | gaa<br>Glu        | ttc<br>Phe<br>840 | ccc<br>Pro | cga<br>Arg        | gag<br>Glu        | 2548 |
| cgg<br>Arg        | ctg<br>Leu<br>845 | cac<br>His        | ctg<br>Leu | Gly<br>999 | aga<br>Arg        | gtg<br>Val<br>850 | ctc<br>Leu        | ggc<br>Gly | tac<br>Tyr | ggc<br>Gly        | gcc<br>Ala<br>855 | ttc<br>Phe        | ggg<br>Gly | aag<br>Lys        | gtg<br>Val        | 2596 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | gac<br>Asp        |                   | 2644 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | cac<br>His<br>890 |                   | 2692 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | cac<br>His        |                   | 2740 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | ccc<br>Pro        |                   | 2788 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | ttc<br>Phe        |                   | 2836 |
| _                 | _                 | _                 |            | _          | _                 |                   | -                 |            | _          |                   |                   | _                 |            | ccc<br>Pro        | -                 | 2884 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | gat<br>Asp<br>970 |                   | 2932 |
|                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   |                   |            | tcg<br>Ser        |                   | 2980 |

| acc gag ggc gga gcg agg cgg gct tct cca gac caa gaa gct gag gac<br>Thr Glu Gly Gly Ala Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp<br>990 995 1000        | 3028 |
|---|------|
| ctg tgg ctg agc ccg ctg acc atg gaa gat ctt gtc tgc tac agc ttc<br>Leu Trp Leu Ser Pro Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe<br>1005 1010 1015      | 3076 |
| cag gtg gcc aga ggg atg gag ttc ctg gct tcc cga aag tgc atc cac<br>Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His<br>1020 1025 1030 1035 | 3124 |
| aga gac ctg gct gct cgg aac att ctg ctg tcg gaa agc gac gtg gtg<br>Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val<br>1040 1045 1050      | 3172 |
| aag atc tgt gac ttt ggc ctt gcc cgg gac atc tac aaa gac cct gac<br>Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp<br>1055 1060 1065      | 3220 |
| tac gtc cgc aag ggc agt gcc cgg ctg ccc ctg aag tgg atg gcc cct<br>Tyr Val Arg Lys Gly Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro<br>1070 1075 1080      | 3268 |
| gaa age ate tte gae aag gtg tae ace acg cag agt gae gtg tgg tee<br>Glu Ser Ile Phe Asp Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser<br>1085 1090 1095      | 3316 |
| ttt ggg gtg ctt ctc tgg gag atc ttc tct ctg ggg gcc tcc ccg tac<br>Phe Gly Val Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr<br>1100 1105 1110 1115     | 3364 |
| cct ggg gtg cag atc aat gag gag ttc tgc cag cgg ctg aga gac ggc<br>Pro Gly Val Gln Ile Asn Glu Glu Phe Cys Gln Arg Leu Arg Asp Gly<br>1120 1125 1130      | 3412 |
| aca agg atg agg gcc ccg gag ctg gcc act ccc gcc ata cgc cgc atc<br>Thr Arg Met Arg Ala Pro Glu Leu Ala Thr Pro Ala Ile Arg Arg Ile<br>1135 1140 1145      | 3460 |
| atg ctg aac tgc tgg tcc gga gac ccc aag gcg aga cct gca ttc tcg<br>Met Leu Asn Cys Trp Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser<br>1150 1155 1160      | 3508 |
| gag ctg gtg gag atc ctg ggg gac ctg ctc cag ggc agg ggc ctg caa<br>Glu Leu Val Glu Ile Leu Gly Asp Leu Leu Gln Gly Arg Gly Leu Gln<br>1165 1170 1175      | 3556 |
| gag gaa gag gag gtc tgc atg gcc ccg cgc agc tct cag agc tca gaa<br>Glu Glu Glu Glu Val Cys Met Ala Pro Arg Ser Ser Gln Ser Ser Glu<br>1180 1185 1190 1195 | 3604 |
| gag ggc agc ttc tcg cag gtg tcc acc atg gcc cta cac atc gcc cag<br>Glu Gly Ser Phe Ser Gln Val Ser Thr Met Ala Leu His Ile Ala Gln<br>1200 1205 1210      | 3652 |

| gct gac gct gag gac agc ccg cca agc ctg cag cgc cac agc ctg gcc 3700 Ala Asp Ala Glu Asp Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala 1215 1220 1225       | Í |
|---|---|
| gcc agg tat tac aac tgg gtg tcc ttt ccc ggg tgc ctg gcc aga ggg 3748 Ala Arg Tyr Tyr Asn Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly 1230 1235 1240       | ) |
| gct gag acc cgt ggt tcc tcc agg atg aag aca ttt gag gaa ttc ccc 3796 Ala Glu Thr Arg Gly Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro 1245 1250 1255       | į |
| atg acc cca acg acc tac aaa ggc tct gtg gac aac cag aca gac agt 3844 Met Thr Pro Thr Thr Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser 1260 1265 1270 1275  | 1 |
| ggg atg gtg ctg gcc tcg gag gag ttt gag cag ata gag agc agg cat 3892 Gly Met Val Leu Ala Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His 1280 1285 1290       | 2 |
| aga caa gaa agc ggc ttc agc tgt aaa gga cct ggc cag aat gtg gct 3940<br>Arg Gln Glu Ser Gly Phe Ser Cys Lys Gly Pro Gly Gln Asn Val Ala<br>1295 1300 1305 | ) |
| gtg acc agg gca cac cct gac tcc caa ggg agg cgg cgg cgg cct gag Val Thr Arg Ala His Pro Asp Ser Gln Gly Arg Arg Arg Pro Glu 1310 1315 1320                | 3 |
| cgg ggg gcc cga gga ggc cag gtg ttt tac aac agc gag tat ggg gag 4036<br>Arg Gly Ala Arg Gly Gly Gln Val Phe Tyr Asn Ser Glu Tyr Gly Glu<br>1325 1330 1335 | 5 |
| ctg tcg gag cca agc gag gag gac cac tgc tcc ccg tct gcc cgc gtg Leu Ser Glu Pro Ser Glu Glu Asp His Cys Ser Pro Ser Ala Arg Val 1340 1345 1350 1355       | ł |
| act ttc ttc aca gac aac agc tac taagcagcat cggacaagac ccccagcact 4138<br>Thr Phe Phe Thr Asp Asn Ser Tyr<br>1360  | 3 |
| tgggggttca ggcccggcag ggcgggcaga gggctggagg cccaggctgg gaactcatct 4198  | 3 |
| ggttgaactc tggtggcaca ggagtgtcct cttccctctc tgcagacttc ccagctagga 4258  |   |
| agagcaggac tccaggccca aggctcccgg aattccgtca ccacgactgg ccagggcacg 4318  |   |
| ctccagctgc cccggcccct ccccctgaga ttcagatgtc atttagttca gcatccgcag 4378  |   |
| gtgctggtcc cggggccagc acttccatgg gaatgtctct ttggcgacct cctttcatca 4438  |   |
| cactgggtgg tggcctggtc cctgttttcc cacgaggaat ctgtgggtct gggagtcaca 4498 cagtgttgga ggttaaggca tacgagagca gaggtctccc aaacgccctt tcctcctcag 4558             |   |
| gcacacaget actetececa egagggetgg etggeeteac ecacecetge acagttgaag 4618  |   |
| ggaggggctg tgtttccatc tcaaagaagg catttgcagg gtcctcttct gggcctgacc 4678  |   |
| aaacagccaa ctagcccctg gggtggccac cagtatgaca gtattatacg ctggcaacac 4738  | 8 |

<210> 4 <211> 1363 <212> PRT <213> Homo sapiens

Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu 20 25 30

Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser  $\tt 35 \tt 40 \tt 45$ 

Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala 50 60

Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val 65 70 75 80

Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu 85 90 95

Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110

Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser 115 120 125

Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp 130 135 140

Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val 145 150 155 160

Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu 165 170 175

Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu 180 185 190

Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr 195 200 205

Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile 210 215 220

Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu 225 230 235 240

Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala 245 250 255

Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln 260 265 270

Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His 275 280 285

Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp 290 295 300

Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg 305 310 315 320

Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu 325 330 335

Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val

Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp 355 360 365

Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu

Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala 385 390 395 400

Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu 405 410 415

Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro 420 425 430

Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr 435 440 445

Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr 450 455 460

Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln 465 470 475 480

Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp 485 490 495

Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu 500 505 510

Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val 515 520 525

Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu 530 535 540

Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile 545 550 555 560

Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu 565 570 575 Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg 580 585 590

Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu 595 600 605

Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu 610 620

Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile 625 630 635 640

Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
645
650
655

Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val 660 665 670

Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu 675 680 685

Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala 690 695 700

His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu 705 710 715 720

Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
725 730 735

Arg Val Arg Glu Glu Asp Ala Gly Arg Tyr Leu Cys Ser Val Cys Asn
740 745

Ala Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser 755 760 765

Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val 770 780

Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met 785 790 795 800

Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile 805 810 815

Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser 820 825 830

Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly 835 840 845

Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala 850 855 860

Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met 865 870 875 880

Leu Lys Glu Gly Ala Thr Ala Ser Glu His Arg Ala Leu Met Ser Glu 885 890 895

- Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu 900 905 910
- Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu 915 920 925
- Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp 930 935 940
- Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe 945 950 955 960
- Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser 965 970 975
- Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala 980 985 990
- Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro 995 1000 1005
- Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg Gly 1010 1015 1020
- Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala 025 1030 1035 1040
- Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile Cys Asp Phe \$1045\$
- Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
  1060 1065 1070
- Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asp 1075 1080 1085
- Lys Val Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu 1090 1095 1100
- Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Gln Ile 105 1110 1115 1120
- Asn Glu Glu Phe Cys Gln Arg Leu Arg Asp Gly Thr Arg Met Arg Ala 1125 1130 1135
- Pro Glu Leu Ala Thr Pro Ala Ile Arg Arg Ile Met Leu Asn Cys Trp 1140 1145 1150
- Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe Ser Glu Leu Val Glu Ile 1155 \$1160\$
- Leu Gly Asp Leu Gln Gly Arg Gly Leu Gln Glu Glu Glu Val 1170 1175 1180
- Cys Met Ala Pro Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser 185 1190 1195 1200
- Gln Val Ser Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp 1205 1210 1215

Ser Pro Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn 1220 1225 1230

Trp Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly 1235 1240 1245

Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr Thr 1250 1255 1260

Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val Leu Ala 265 1270 1275 1280

Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln Glu Ser Gly 1285 1290 1295

Phe Ser Cys Lys Gly Pro Gly Gln Asn Val Ala Val Thr Arg Ala His

Pro Asp Ser Gln Gly Arg Arg Arg Pro Glu Arg Gly Ala Arg Gly
1315 1320 1325

Gly Gln Val Phe Tyr Asn Ser Glu Tyr Gly Glu Leu Ser Glu Pro Ser 1330 1335 1340

Glu Glu Asp His Cys Ser Pro Ser Ala Arg Val Thr Phe Phe Thr Asp 1350 1355 1360

Asn Ser Tyr

<210> 5

<211> 1311

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<213> Homo sapiens (FLT1)

<400> 5

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser 1 5 10 15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro 20 25 30

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr 35 40 45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro 50 55 60

Glu Asn Asn Asn Asn Asn Met Val Ser Lys Glu Ser Glu Arg Leu 65 70 75 80

Ser Ile Thr Lys Ser Ala Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser 85 90 95

Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn His Thr Gly Phe Tyr Ser

Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys Glu Thr Glu Ser 115 120 125 Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu 155 Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys 165 170 Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile 200 Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr 215 220 Asn Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr 265 Trp Ser Tyr Pro Asp Asn Asn Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser 295 Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val 325 His Ile Tyr Asp Lys Ala Phe Ile Thr Val Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val Trp Leu Lys Asp Gly Leu 375 380 Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala Gly Asn Tyr Thr Ile Leu 405 Leu Ser Ile Lys Gln Ser Asn Val Phe Lys Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser Arg Gln Ile Leu Thr Cys 455 Thr Ala Tyr Gly Ile Pro Gln Pro Asn Thr Ile Lys Trp Phe Trp His 475 Pro Cys Asn His Asn His Ser Glu Ala Arg Cys Asp Phe Cys Ser Asn 490 Asn Glu Glu Ser Phe Ile Leu Asp Asn Asn Asn Asn Asn Asn Asn Ala Asp Ser Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp 535 Ser Arg Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly 570 Phe His Val Asn Leu Glu Lys Met Pro Thr Asn Asn Glu Gly Glu Asp Leu Lys Leu Ser Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr 600 615 Asn Asn Asn Asn Asn Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu 650 Asn Leu Thr Ile Met Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala 665 Cys Arg Ala Arg Asn Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys 680 Glu Ile Thr Ile Arg Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr

Leu Phe Ile Glu Arg Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys 760

765

- Lys Ala Thr Asn Gln Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr 770 775 780
- Val Gln Gly Thr Ser Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr 785 790 795 800
- Cys Thr Cys Val Ala Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Leu 805 810 815
- Ile Arg Lys Met Lys Arg Ser Ser Asn Ser Glu Ile Lys Thr Asp Tyr 820 825 830
- Leu Ser Ile Ile Met Asp Pro Asp Glu Val Pro Leu Asp Glu Gln Cys 835 840 845
- Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg 850 855 860
- Leu Lys Leu Gly Lys Ser Leu Gly Arg Gly Ala Phe Gly Lys Val Val 865 870 875 880
- Gln Ala Ser Ala Phe Gly Ile Lys Lys Ser Pro Thr Cys Arg Thr Val 885 890 895
- Ala Val Lys Met Leu Lys Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala 900 905 910
- Leu Met Thr Glu Leu Lys Ile Leu Thr His Ile Gly His His Leu Asn 915 920 925
- Val Val Asn Leu Gly Ala Cys Thr Lys Gln Gly Gly Pro Leu Met 930 935 . 940
- Val Ile Val Glu Tyr Cys Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys 945 950 955 960
- Ser Lys Arg Asp Leu Phe Phe Leu Asn Lys Asp Ala Ala Leu His Met 965 970 975
- Glu Pro Lys Lys Glu Lys Met Glu Pro Gly Leu Glu Gln Gly Lys Lys 980 985 990
- Pro Arg Leu Asp Ser Val Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly 995 \$1000\$ 1005
- Phe Gln Glu Asp Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Asp Ser 1010 \$1020\$
- Asp Gly Phe Tyr Lys Glu Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr 1025 1030 1035 1040
- Ser Phe Gln Val Ala Arg Gly Met Glu Phe Leu Ser Ser Arg Lys Cys  $1045 \hspace{1.5cm} 1050 \hspace{1.5cm} 1055$
- Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn 1060 1065 1070
- Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn 1075 \$1080\$

Pro Asp Tyr Val Arg Lys Gly Asp Thr Arg Leu Pro Leu Lys Trp Met 1090 1095 1100

Ala Pro Glu Ser Ile Phe Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val 1105 1110 1115 1120

Trp Ser Tyr Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser 1125 1130 1135

Pro Tyr Pro Gly Val Gln Met Asp Glu Asp Phe Cys Ser Arg Leu Arg 1140 1145 1150

Glu Gly Met Arg Met Arg Ala Pro Glu Tyr Ser Thr Pro Glu Ile Tyr 1155 1160 1165

Gln Ile Met Leu Asp Cys Trp His Arg Asp Pro Lys Glu Arg Pro Arg 1170 1175 1180

Phe Ala Glu Leu Val Glu Lys Leu Gly Asp Leu Leu Gln Ala Asn Val 1185 1190 1195 1200

Gln Gln Asp Gly Lys Asp Tyr Ile Pro Ile Asn Ala Ile Leu Thr Gly 1205 1210 1215

Asn Ser Gly Phe Thr Tyr Ser Thr Pro Ala Phe Ser Glu Asp Phe Phe 1220 1225 1230

Lys Glu Ser Ile Ser Ala Pro Lys Phe Asn Ser Gly Ser Ser Asp Asp 1235 1240 1245

Val Arg Tyr Val Asn Ala Phe Lys Phe Met Ser Leu Glu Arg Ile Lys 1250 \$1255\$

Thr Phe Glu Glu Leu Leu Pro Asn Ala Thr Ser Met Phe Asp Asp Tyr 1265 1270 1275 1280

Gln Gly Asp Ser Ser Thr Leu Leu Ala Ser Pro Met Leu Lys Arg Phe 1285 1290 1295

Thr Trp Thr Asp Ser Lys Pro Lys Ala Ser Leu Lys Ile Glu Val 1300 \$1305 1310

<210> 6

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> The amino acid at positions 1 and 2 each are selected independently from the group consisting of aspartic acid and glutamic acid.

<220>

<223> The amino acid at position 4 is independently selected from the group consisting of methionine and valine.

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<223> The amino acid at position 5 is independently
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      aspartic acid, and glutamic acid.
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 1
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                                                                    70
gactcctgga
<210> 8
<211> 24
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<213> Artificial Sequence
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<223> Description of Artificial Sequence:
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                                                                    24
<210> 9
<211> 22
<212> DNA
<213> Artificial Sequence
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<213> Artificial Sequence
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| <220> <223> Description of Artificial Sequence: oligonucleotide probe   |        |
|---|--------|
| <400> 10 ccatcgatgg atcctacctg aagccgcttt ctt                           | 33     |
| <210> 11<br><211> 34<br><212> DNA<br><213> Artificial Sequence          |        |
| <220> <223> Description of Artificial Sequence: oligonucleotide probe   |        |
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| <210> 12<br><211> 20<br><212> DNA<br><213> Artificial Sequence          |        |
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| <400> 12<br>gttgcctgtg atgtgcacca                                       | 20     |
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| <400> 13<br>ctggagtcga cttggcggac t                                     | 21     |
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                                                                    21
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| <400> 19<br>ctggagtcga cttggcggac t  |  |  |  |  |  |  |  |  |  |  |
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| <400> 20<br>egeggateca agettaetta eetteeatge tgecettate eteg                             |  |  |  |  |  |  |  |  |  |  |
| <210> 21<br><211> 419<br><212> PRT<br><213> Homo sapiens                                 |  |  |  |  |  |  |  |  |  |  |
| <400> 21<br>Met His Leu Leu Gly Phe Phe Ser Val Ala Cys Ser Leu Leu Ala Ala<br>1 5 10 15 |  |  |  |  |  |  |  |  |  |  |
| Ala Leu Leu Pro Gly Pro Arg Glu Ala Pro Ala Ala Ala Ala Phe 20 25 30                     |  |  |  |  |  |  |  |  |  |  |
| Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu Ala<br>35 40 45              |  |  |  |  |  |  |  |  |  |  |
| Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser<br>50 60                 |  |  |  |  |  |  |  |  |  |  |
| Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys Met 65 70 75 80              |  |  |  |  |  |  |  |  |  |  |
| Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu Gln 85 90 95                 |  |  |  |  |  |  |  |  |  |  |
| Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala 100 105 110              |  |  |  |  |  |  |  |  |  |  |
| His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys 115 120 125              |  |  |  |  |  |  |  |  |  |  |
| Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe 130 140                  |  |  |  |  |  |  |  |  |  |  |
| Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val Tyr 145 150 155 160          |  |  |  |  |  |  |  |  |  |  |
| Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr<br>165 170 175           |  |  |  |  |  |  |  |  |  |  |
| Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu<br>180 185 190           |  |  |  |  |  |  |  |  |  |  |

Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser 195 200 205

Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile 210 215 220

Ile Arg Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Asn225230240

Lys Thr Cys Pro Thr Asn Tyr Met Trp Asn Asn His Ile Cys Arg Cys 245 250 255

Leu Ala Gl<br/>n Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser 260 265 270

Thr Asp Gly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu 275 280 285

Glu Thr Cys Gln Cys Val Cys Arg Ala Gly Leu Arg Pro Ala Ser Cys 290 295 300

Gly Pro His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys 305 310 315 320

Asn Lys Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu 325 330 335

Asn Thr Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro 340 350

Leu Asn Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys 355 360 365

Cys Leu Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr 370 375 380

Arg Arg Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser 385 390 395 400

Tyr Ser Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro 405 410 415

Gln Met Ser

<210> 22

<211> 354

<212> PRT

<213> Homo sapiens

<400> 22

Met Tyr Arg Glu Trp Val Val Val Asn Val Phe Met Met Leu Tyr Val 1 5 10 15

Gln Leu Val Gln Gly Ser Ser Asn Glu His Gly Pro Val Lys Arg Ser 20 25 30

- Ser Gln Ser Thr Leu Glu Arg Ser Glu Gln Gln Ile Arg Ala Ala Ser 40 45
- Ser Leu Glu Glu Leu Leu Arg Ile Thr His Ser Glu Asp Trp Lys Leu 50 55 60
- Trp Arg Cys Arg Leu Arg Leu Lys Ser Phe Thr Ser Met Asp Ser Arg 65 70 75 80
- Ser Ala Ser His Arg Ser Thr Arg Phe Ala Ala Thr Phe Tyr Asp Ile 85 90 95
- Glu Thr Leu Lys Val Ile Asp Glu Glu Trp Gln Arg Thr Gln Cys Ser 100 105 110
- Pro Arg Glu Thr Cys Val Glu Val Ala Ser Glu Leu Gly Lys Ser Thr 115 120 125
- sn Thr Phe Phe Lys Pro Pro Cys Val Asn Val Phe Arg Cys Gly Gly 130 \$140\$
- Cys Cys Asn Glu Glu Ser Leu Ile Cys Met Asn Thr Ser Thr Ser Tyr 145 150 155 160
- Ile Ser Lys Gln Leu Phe Glu Ile Ser Val Pro Leu Thr Ser Val Pro 165 170 175
- Glu Leu Val Pro Val Lys Val Ala Asn His Thr Gly Cys Lys Cys Leu 180 185 190
- Pro Thr Ala Pro Arg His Pro Tyr Ser Ile Ile Arg Arg Ser Ile Gln
  195 200 205
- Ile Pro Glu Glu Asp Arg Cys Ser His Ser Lys Lys Leu Cys Pro Ile 210 215 220
- Asp Met Leu Trp Asp Ser Asn Lys Cys Lys Cys Val Leu Gln Glu Glu 225 230 235
- Asn Pro Leu Ala Gly Thr Glu Asp His Ser His Leu Gln Glu Pro Ala 245 250 255
- Leu Cys Gly Pro His Met Met Phe Asp Glu Asp Arg Cys Glu Cys Val 260 265 270
- Cys Lys Thr Pro Cys Pro Lys Asp Leu Ile Gln His Pro Lys Asn Cys 275 280 285
- Ser Cys Phe Glu Cys Lys Glu Ser Leu Glu Thr Cys Cys Gln Lys His 290 295 300
- Lys Leu Phe His Pro Asp Thr Cys Ser Cys Glu Asp Arg Cys Pro Phe 305 310 315 320
- His Thr Arg Pro Cys Ala Ser Gly Lys Thr Ala Cys Ala Lys His Cys 325 330 335
- Arg Phe Pro Lys Glu Lys Arg Ala Ala Gln Gly Pro His Ser Arg Lys 340 345 350